IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Alan R. Fritzberg et al.	Examiner: Unknown
Serial No.:	Unknown	Group Art Unit: Unknown
Filed:	June 12, 2000	Docket: 295.044US1
Title:	HIGH DOSE RADIONUCLIDE COMPLEXES FOR BONE MARROW SUPPRESSION	

PRELIMINARY AMENDMENT

BOX PATENT APPLICATION
Commissioner for Patents
Washington, D.C. 20231

Prior to examination, please amend the above-identified patent application as follows:

IN THE SPECIFICATION

On page 1, after the title, please insert the following:

--RELATED APPLICATION

This is a continuation under 37 CFR § 1.11(a) of PCT Application Serial No. PCT/US00/16052, filed on June 12, 2000 and published as WO 00/76556 on December 21, 2000, which claims priority from provisional U.S. Patent Application No. 60/139,065, filed June 11, 1999, 60/143,780, filed June 13, 1999 and 60/149,821, filed August 19, 1999, all of which applications are incorporated herein by reference.--

IN THE CLAIMS

Please substitute the claim set in the appendix entitled Clean Version of Pending Claims for the previously pending claim set. The substitute claim set is intended to reflect cancellation of claims 1-85 and addition of new claims 86-105. The specific amendments to individual claims are detailed in the following marked up set of claims.

86. A therapeutic method for treating a bone-associated cancer comprising:

(a) hydrating said cancer patient by administration of water;

(b) parenterally administering a single dose of ^{166}Ho-DOTMP to said patient in an aqueous vehicle comprising an effective antiradiolytic amount of a pharmaceutically acceptable radioprotectant, said dose being effective to deliver about 20-60 Gy to the bone marrow of said patient;

(c) administering a dose of at least about 200 mg/m^2 melphalan to the patient; and

(d) providing the patient with an autologous stem cell transplant;

wherein the patient is not subjected to total body irradiation in conjunction with the therapeutic method.

87. The method of claim 86 wherein the cancer is multiple myeloma.

88. The method of claim 86 wherein the cancer is metastatic breast or prostate cancer.

89. The method of claim 86 wherein the cancer is Ewing's sarcoma.

90. The method of claim 86, 87 or 88 wherein the radioprotectant is ascorbic acid or gentisic acid.

91. The method of claim 90 wherein the concentration of ascorbic acid is about 35-75 mg/ml.

92. The method of claim 91 wherein the vehicle is buffered to about pH 7-8.

93. The method of claim 90, 91 or 92 wherein the dose is effective to deliver about 20-30 Gy to the bone marrow of said patient.

94. A method to prepare a medicament for the treatment of bone-associated cancer comprising combining ^{166}Ho-DOTMP in an aqueous vehicle with an effective antiradiolytic amount of a pharmaceutically acceptable radioprotectant, wherein said medicament is effective to deliver a dose of about 20-60 Gy to the bone marrow of said patient in a single infused dose.

95. The use of claim 94 wherein the radioprotectant is ascorbic acid or gentisic acid.

96. The method of claim 94 or 95 wherein the vehicle is buffered to about pH 7-8.

97. The method of claim 94 wherein the cancer is multiple myeloma.

98. The method of claim 94 wherein the cancer is Ewing's sarcoma.

99. The method of claim 94 wherein the cancer is metastatic breast or prostate cancer.

100. A liquid pharmaceutical composition comprising ^{166}Ho complexed with 1,4,7,10-tetraazacyclododecanetetramethylene-phosphonic acid (DOTMP) and an effective antiradiolytic amount of a pharmaceutically acceptable radiprotectant.

101. The composition of claim 100, wherein the radioprotectant is ascorbic acid or gentisic acid.

102. The composition of claim 101 comprising about 35-75 mg ascorbic acid/ml of composition.

103. The composition of claim 100 or 101 wherein the ratio of DOTMP to ^{166}Ho is above 3.

104. The composition of claim 100, comprising an aqueous carrier adjusted to pH 7-8.

105. The composition of claim 100 which is stable for at least 72 hours under ambient conditions.

REMARKS

The above-identified continuation application has been amended to cancel claims 1-85 and add new claims 86-105. No new matter has been added. The claims are supported throughout the specification and by the originally filed claims in the PCT.

The Examiner is invited to call Applicant's attorney if there are any questions concerning this application.

Respectfully submitted,

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